Citation:

Frost L, Vestergaard P. n-3 Fatty acids consumed from fish and risk of atrial fibrillation or flutter: the Danish Diet, Cancer and Health Study. *Am J Clin Nutr*. 2005; 81: 50-54.

PubMed ID: 15640459

Study Design:

Retrospective cohort study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the association between consumption of n-3 fatty acids from fish and risk of incident atrial fibrillation or flutter.

Inclusion Criteria:

Participants enrolled in the Danish Diet, Cancer, and Health Study (a prospective cohort study with the primary aim of studying the role of diet in cancer risk).

Exclusion Criteria:

- Patients with a previous cancer diagnosis and patients who had been hospitalized before baseline with endocrine disorders or cardiovascular diseases other than hypertension were excluded
- Patients taking medication for ischemic heart disease, stroke or diabetes were excluded.

Description of Study Protocol:

Recruitment

Participants enrolled in the Danish Diet, Cancer, and Health Study (a prospective cohort study with the primary aim of studying the role of diet in cancer risk).

Design

Prospective cohort study.

Blinding used

Yes. Investigators used ICD9 codes furnished by diagnosing physician.

Intervention

None (examined food frequency questionnaire and formed cohorts based on fish consumption).

Statistical Analysis

Multivariate Cox regression model by an initial forced entry of known risk factors for atrial fibrillation, namely, age, sex, body height, body mass index (BMI), alcohol consumption, systolic blood pressure, and treatment of hypertension (HTN), followed by forward selection of other variables of interest. Variables in the final model were age, sex, height, BMI, systolic blood pressure, total cholesterol more than six mmol per liter (yes or no), treatment for HTN (yes or no), sex-specific quintile of fish-oil consumption. After, total daily energy intake (kJ per day), frequency of consumption of fatty fish, smoking (never, former or current) and length of education after elementary school. Correlation was evaluated by Spearman's non-parametric correlation analysis. Confidence level was 95%. SPSS version 11.5 was the statistical software.

Data Collection Summary:

Timing of Measurements

Measured at baseline: height, weight, systolic, diastolic blood pressure, non-fasting total cholesterol. Participants completed a questionnaire about medical diseases, including myocardial infarction, angina, stroke, HTN, hypercholesterolemia and diabetes and drug treatment for these conditions, smoking habits, alcohol intake, health and education. The data were compiled by examining the Danish National Registry of Patients in which physicians had coded all events at hospital discharge.

Dependent Variables

- Atrial fibrillation
- Atrial flutter.

Independent Variable

Intake of n-3 fatty acid fish.

Description of Actual Data Sample:

Initial N: 49,949

Age: 55.5±4 to 56.9±4

Ethnicity: Danish

Other relevant demographics: None significant

Anthropometrics: No statistical difference

Location: Denmark.

Summary of Results:

During a follow-up of 5.7 years (mean), atrial fibrillation or flutter had developed in 556 subjects. Consumption of n-3 fatty acids from fish was not associated with a reduction in risk of these events.

Risk of Atrial Fibrillation or Flutter by n-3 PUFA Intake from Fish

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P-Value for Trend
n-3 PUFA intake (g/d)	0.16±0.08	0.36±0.06	0.52±0.07	0.74±0.10	1.29±0.47	
Adjusted hazard ratio (95% CI)	1.00	0.86 (0.65,1.15)	1.08 (0.82,1.42)	1.01 (0.77,1.34)	1.34 (1.02,1.76)	0.006

Author Conclusion:

Consumption of n-3 fatty acids from fish was not associated with a reduction in risk of atrial fibrillation or flutter. The possibility of residual confounding caused by a lack of information on intake of fish-oil tablets cannot be excluded.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes

1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes

4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes

7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	???
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	???
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes